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CUTANEOUS BLOOD FLOW IN PSORIASIS MEASURED BY ^{133}XENON CLEARANCE*

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ABSTRACT

By the radioactive, freely diffusible, inert gas ^{133}Xenon we studied the cutaneous blood flow in 15 cases of fresh, untreated psoriasis and in 10 normal subjects.

In normal skin and in uninvolved skin in psoriatics the blood flow proved to be approx. 6.5 ml/100 g tissue per min, while in the psoriatic plaques it was twice this value, *viz.*, about 12 ml/100 g tissue per min.

It is concluded (1) that the gross erythema, the slightly elevated skin temperature (by 1.5° C), and the microscopic evidence of vascular changes in psoriatic lesions are in fact based upon increased blood flow, (2) that, according to the results of the present technique, the cutaneous tissue of uninvolved skin in psoriatics does not have a greater blood flow than cutaneous tissue of controls, and (3) that the present method of determining the cutaneous blood flow following intracutaneous injection of ^{133}Xenon, calculating from the first, rapidly falling slope of the flow curve, is well-suited for clinical use, as the measurement need not be done for more than 10–15 minutes in order to calculate the cutaneous blood flow during the traumatic phase immediately after the injection.

Van Scott and Ekel (1), demonstrated an increased cell turnover rate of up to tenfold in psoriasis. The erythema and the easily felt increase in temperature in the psoriatic lesion gives the impression that the blood flow in psoriatic plaques is considerably greater than in normal skin. In microscopic studies of the capillaries Illig and Koops (2), among others, found elongated and tortuous cutaneous capillaries in the psoriatic lesions as well as development of numerous new capillaries.

The object of our study was to determine the blood flow in psoriatic plaques, in the normal appearing skin of psoriatics, and in the skin of normal subjects, measured directly in ml per 100 grams tissue per minute.

MATERIALS AND METHODS

The material primarily was comprised of 15 psoriatics and 10 normal subjects. The tests were performed on patients with a flare up of psoriasis or newly diagnosed psoriasis, all untreated for at least the past two weeks. Only patients with scattered nummular psoriatic lesions on the trunk and limbs were included. No patient or control had hypertension, abnormal pulse rate, metabolic disease, or diabetes mellitus, and none had smoked during the 2 hours before the test.

In psoriatics the blood flow was measured in fresh psoriatic lesions on the limbs. For comparison, the blood flow in clinically normal appearing skin in these patients was studied in a symmetrical region. In the normal subjects the blood flow in the skin was measured on the volar aspect of the forearm. Patients and controls were comparable in respect to sex and age, and the measurements were carried out under the same external circumstances.

The temperature in the room and the relative humidity were 22 ± 1° C and 60 ± 10% respectively. Patients as well as controls with a visible or perceptible sweating tendency were excluded. Before the test the pulse rate and skin temperature were measured in the psoriatic lesion as well as in the normal skin where the blood flow was to be measured. After the patients had been reclining for approx. 30 minutes under stable circumstances the measurement was carried out.

The injection technique of Sejrsen (3, 4) was used. With a Hamilton syringe, needle diameter 0.25 mm, 0.03 ml radioactive Xenon-133 (^{133}Xe) in a 0.9% NaCl solution, 1.0 mCi/ml (Atomenergi, Nyköbing, Sweden) was injected intracutaneously. The needle was inserted obliquely 3–5 mm intracutaneously, and the test was performed as an ordinary intracutaneous test, e.g. tuberculin test.

The radioactivity was measured with a Philips Detector 4111, Philips Supply Unit PW 4022, Philips Ratemeter 4042, and a Potentiometric Linear Recorder PR 2500. For practical reasons we tried to obtain the same starting point of the Xenon clearance curves by varying the detector-skin distance. This distance averaged 11.9 cm. The appa-

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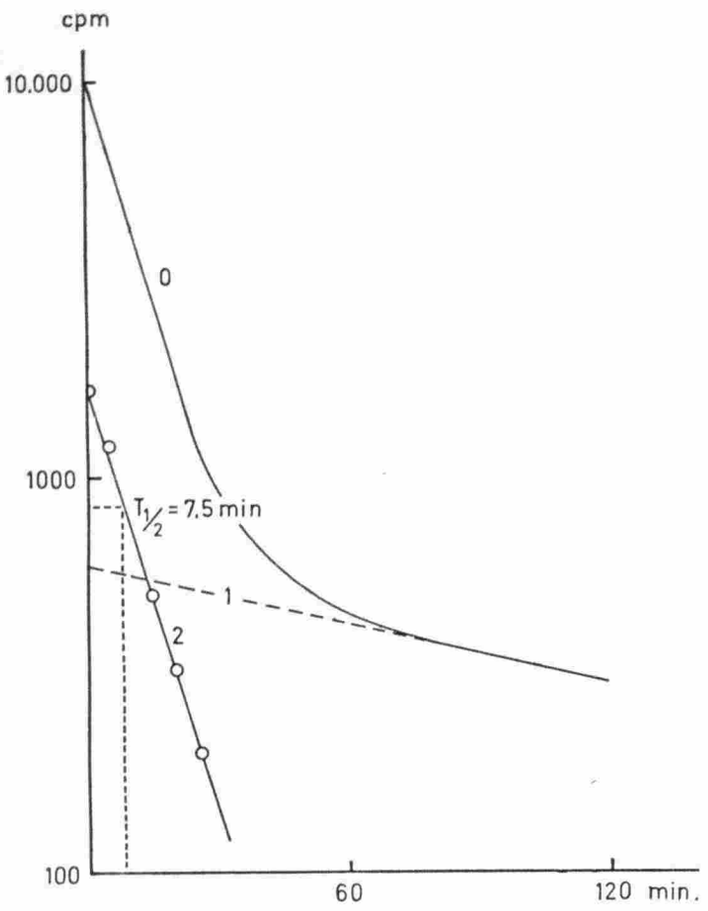

FIG. 1. Diagram illustrating the ^{133}Xe elimination curve. The faster of the two components of the composite curve is used in calculating the skin blood flow.

ratus was calibrated before and after each use. The curves were traced for approx. 30 minutes after the injection of ^{133}Xe. After correction for background, it is possible to calculate, in a semilogarithmic system, the blood flow, F, from the fall of the initial, rectilinear part of the curve using the formula:

$$F = \frac{\ln 2 \times \lambda \times 100}{T_{\frac{1}{2}}} \text{ ml/100 g/min}$$

where ln 2 is the natural logarithm of 2 (0.693); $\lambda = 0.7$ is the experimentally demonstrated tissue to blood partition coefficient, as muscle, hepatic, renal, and cutaneous tissue show the same per cent distribution of water, proteins, and lipid (5, 6, 4). $T_{1/2}$ is the half-time of the cutaneous ^{133}Xe depot found in the test.

During the elimination of Xenon from the skin the cutaneous venous blood gives off a small part of the tracer to the subcutaneous fatty tissue, which has a great affinity for Xenon. This part will be washed out from the subcutaneous tissue with the blood. The λ for Xenon in fatty tissue being about 15 times greater than in cutaneous tissue, the washout curves will show a considerably slower fall after the first 30 minutes or so.

To ascertain the influence of this lipid binding upon the calculations of the cutaneous blood flow, another 7 psoriatics and 5 controls were tested. In these cases two-hour curves of the ^{133}Xe clearance from the injected depot were plotted. As shown in Fig. 1 the calculation of the cutaneous blood flow in these experiments was done by back extrapolating the tail part of the curve to zero time and then substracting this curve from that recorded (curve 0). This gives a new curve whose initial slope indicates the washout of ^{133}Xe from the cutaneous tissue during the traumatic, initial phase. From this initial slope the cutaneous blood flow may be calculated (3, 4).

RESULTS

The results of the measurements over 30 minutes, the blood flow being calculated from the initial slopes of the curves, are presented in Table I. The mean skin blood flow of the normal subjects was found to be 6.5 ml/100 g/min. The corresponding value for the psoriatic lesions in the psoriatic patients was 12.1 ml/100 g/min., i.e. twice that in the normal series.

The blood flow in the normal-looking skin of psoriatic patients was found to correspond to that in the normal series, averaging 6.3 ml/100 g/min. The difference between the flows in psoriatic plaques and in the uninvolved skin of psoriatics is significant, $p < 0.01$.

Calculations on the basis of the two-hour curves (Table II) showed in the 5 normal subjects an average cutaneous flow of 6.6 ml/100 g/min and in the 7 psoriatics a mean flow of 12.8 ml/100 g/min. The difference between these two latter mean flows is significant, $p < 0.001$.

DISCUSSION

^{133}Xe was injected intracutaneously. In principle, therefore, measuring errors may occur by reflux through the injection path or in the presence of a defect in the epidermis. Attempts were made to reduce these errors. In the first place, very fine needles were used. Secondly, the site of injection was cautiously wiped with soft tissue paper immediately after the injection and before starting the measurement, and thereafter the tissue paper was removed far from the area. Thirdly, diffusion, if any, through the skin was assessed by performing an experiment on two patients and controls, measuring symmetrical injection sites, with and without a thin aluminium foil cover. This gave identical flow curves for psoriatic plaques as well as for normal skin.

TABLE I

Blood flow calculated from the initial slope in curves recorded for 20–30 minutes

Patients			Skin blood flow (ml/100 g × min)		Skin temperature			Controls			Skin blood flow
No./name	Age	Sex	normal	psoriasis	normal	psoriasis	diff.	No./name	Age	Sex	
1. H.O.	64	m	6.5	8.8	31.6	33.0	1.4	1. N.D.	48	f	3.1
2. S.C.	23	m	16.2	24.3	31.0	32.5	1.5	2. V.H.	58	f	4.4
3. F.M.	66	m	8.8	13.9	33.0	35.5	2.5	3. E.J.	67	f	5.4
4. A.L.	59	f	4.1	6.6	32.0	34.0	2.0	4. J.N.	41	f	6.1
5. A.N.	18	f	3.7	6.5	32.0	33.0	1.0	5. N.M.	31	m	6.1
6. S.P.	13	f	3.5	6.4	31.0	31.5	0.5	6. N.C.	42	f	7.5
7. E.H.	44	m	6.8	12.1	31.5	35.0	3.5	7. N.M.	27	f	8.1
8. J.P.	36	f	4.8	9.7	34.0	35.0	1.0	8. N.W.	62	m	8.1
9. H.B.	56	m	13.1	26.9	—	—	—	9. P.N.	18	m	8.5
10. E.L.	59	m	2.0	4.4	33.2	33.4	0.2	10. M.A.	29	m	7.5
11. A.N.	71	f	9.2	20.2	32.6	33.8	1.2				
12. M.L.	14	f	6.1	15.1	33.0	35.0	2.0				
13. A.L.	59	m	3.6	11.8	32.0	33.0	1.0				
14. C.L.	32	f	2.9	10.3	31.8	33.2	1.4				
15. L.P.	32	f	1.1	4.5	32.0	33.5	1.5				
Total	646		92.4	181.5	450.7	471.4	20.7		423		64.8
Mean	43		6.16	12.1	32.2	33.7	1.5		42		6.5
		M	6.16	12.1							
		s^2	17.50	48.34							
		σ	5.73								
		t	3.06								
		$0.01 > p > 0.001$									

TABLE II

Cutaneous blood flow calculated from the fast component in curves recorded for two hours

Patients			Cutaneous blood flow (ml./100 g. × min.)		Controls			Cutaneous blood flow	
No./Name	Age	Sex	Right arm	Left arm	No./Name	Age	Sex		
1. O.L.	15	m	16.1	12.1	1. W.L.	57	m	7.0	
2. B.A.	22	f	11.4	12.9	2. H.R.	41	m	4.0	6.0
3. J.R.	84	m	11.4	11.0	3. Å.R.	77	m	7.0	7.0
4. A.L.	26	m	13.8	13.8	4. A.N.	32	m	7.4	7.0
5. E.P.	23	m	11.4	12.1	5. H.J.	42	m	8.0	6.0
6. I.N.	35	f	16.1	12.1					
7. I.B.	16	m	12.1	12.9					
Total	221		179.2			249		59.4	
Mean	32		12.8			50		6.6	
M			12.8					6.60	
s^2			2.68					1.34	
σ					1.46				
t					10.16				
					$p < 0.001$				

The next question which arises is to what extent the local reaction to the injection trauma induces an increased blood flow at the injection site itself. Sejrsen (3) has performed comparative studies of the blood flow measured by non-traumatic epicutaneous application of ^{133}Xe and by intracutaneous application of ^{133}Xe. In 10 normal subjects the epicutaneous application gave a mean value of 5.7 ml/100 g/min, while intracutaneous injection of ^{133}Xe (with histamine added to obtain maximum blood flow) showed a mean value of 10.7 ml/100 g/min. These studies have afforded comparable results which also indicate that the named sources of error are of little importance when ample experience of the technique has been gained. As we did not add histamine to the injected ^{133}Xe, our values would be expected to be between those reported, and they proved to be closer to those found with epicutaneous application of ^{133}Xe.

The formula used for calculating the blood flow is valid presupposing that the tissue has a homogeneous perfusion and that a diffusion equilibrium between tissue and blood has been attained (7).

As described by Sejrsen (3, 4), the flow curve after the first 60 minutes represents mainly subcutaneous accumulation of ^{133}Xe. Since in our measurements we were interested in using a relatively short-lasting and therefore clinically applicable method, we calculated the cutaneous blood flow from the initial slopes of the curves (Table I), knowing that thereby the cutaneous blood flow is underestimated. This method of calculation was used for the first 15 psoriatics and 10 controls. To investigate the extent of this underestimation we did, as already mentioned, two-hour flow measurements on 7 psoriatics and 5 controls (Table II). This showed good agreement between the flow values found by the two methods of calculation.

It may be mentioned that the ^{133}Xe, as used here, is presumably best suited for comparative investigations of the cutaneous blood flow in various types of skin and between normal and diseased skin. Variations in the measuring results may be imagined due to functional vasolability or different blood flow in different regions. Therefore, the method must, as mentioned, be more reliable in comparative studies than in absolute single determinations. These problems have been touched upon by others (8, 9) who expressed the tissue clearance found in the half-time (counts per minute) of ^{24}Na and of that part of ^{131}I which was eliminated per minute. However, these isotopes do not afford a possibility of assessing the blood flow in the tissue, as their diffusion is limited.

Psoriasis research has not yet given the final answer to the question of whether uninvolved skin of psoriatics is normal. On the basis of histological studies of apparently normal skin from psoriatics Madden (10) believed that the epidermal and dermal vascular changes were present also in cutaneous areas which are not visibly affected. Holti (11), in uninvolved skin of psoriatics, found vascular changes so different from the vascular appearances in normals that he felt capable of diagnosing psoriasis before the first eruption of psoriasis. Herdenstam (12) found an increased oxygen uptake in the apparently normal skin of psoriatics.

On the other hand, Yamazaki (13), by capillary microscopy, and Halprin (14), by a study of the glucose metabolism, have found the uninvolved skin of psoriatics to show none of the changes characterizing the psoriatic lesion. Our results are similar in that we found no change in uninvolved skin but a marked increase in the blood flow in the psoriatic plaques corresponding to the demonstrated elevation of skin temperature of 1.5° C (Table I).

The results indicate, moreover, that with the present testing technique blood flow in the cutaneous tissue of uninvolved skin in psoriatics is not increased compared with that found in the cutaneous tissue of controls.

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